The 2010 Health Care Reform Act: A Potential Opportunity to Advance Cancer Research by Taking Cancer Personally

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Abstract

The Patient Protection and Affordable Care Act of 2010 will have a profound influence on health care in the United States, including how we conduct cancer research and cancer care delivery. For this reason, oncologists and researchers must be intimately involved in the implementation and interpretation of this important legislation. A major goal of the Act is to improve access to affordable, quality health care. An important element in achieving this goal will be to learn from patients’ experiences and build the foundation for evidence-based personalized medicine. This will require a partnership among researchers, clinicians, policy makers and regulators, and patients to design an integrated information network system that will be the basis for providing the right treatment for the right patient in the right place at the right time. In this review, we will discuss the salient points of the Act that specifically affect cancer research and care, as well as highlight opportunities for oncologists and researchers to play a primary role in developing a health care system that includes personalized medicine approaches that will in turn enhance the likelihood of achieving the goals and objectives of the health care reform act. Clin Cancer Res; 16(24); 5987–96. ©2010 AACR.
With sufficient forethought and input by cancer researchers, the development of information networks that follow patients over their lifetime will promote evidenced-based approaches to cancer care. Careful tracking of how individual patients with specific molecular alterations in their tumors respond to specific therapies will facilitate a continuous cycle of research and care and will improve clinical decision-making based on the responses of previously treated patients (Fig. 2), as supported by Fojo and Parkinson (14) in this edition of CCR Focus. An evidence-based approach to cancer research and clinical care should be an important element in the evolution of health care reform, and would reduce overall costs by promoting comparative effectiveness research (CER) and health technology assessment (HTA) (15, 16).

Given the technological advances made during the past decade in elucidating the molecular biology of disease, especially cancer, we are now at the threshold of personalizing care and even intervening before disease occurs by identifying populations at risk. To capitalize on what could be a remarkable opportunity to implement a precise system of personalized cancer care, academic physicians and researchers must contribute to the architecture of the reformed approach by (1) recognizing the heterogeneity of cancers and its impact on the development of new diagnostics and treatment strategies; (2) encouraging the development of cancer biomarkers that can identify populations at risk and guide treatment for patients to achieve the largest benefit with the fewest side effects; (3) developing integrated information networks that involve rapid-learning systems to inform decision tools for clinicians and patients, as well as to serve as a basis for novel research strategies, including driving the discovery of new targets in nonresponsive patients; and (4) providing support for well-designed clinical trials that serve unique patient populations, including the underserved and those suffering health disparities.

In this Focus review, we identify and discuss the salient points of PPACA that specifically address cancer care and research. We also highlight what we believe to be an opportunity and need for oncologists and cancer researchers to become strategically involved in developing precise approaches to medical care, and by so doing, not only improve cancer care but make it more affordable by using CER and reducing the element of trial and error. Finally, we discuss how solutions for improving cancer care, and health care in general, must be addressed along several fronts, such as (1) the need to discover new biomarkers that can predict the right treatment for the right patient in the right place at the right time; (2) the need for research to improve patient access to care and insurance coverage, including health disparities research; (3) the need for CER and HTA techniques to integrate novel technologies into the standard of care; and (4) the need to develop a comprehensive information network that embraces rapid learning systems. We provide "use cases" to illustrate how the reformed system could personalize treatment approaches and improve cancer research and patient outcomes.

### Salient Points of PPACA that Affect Cancer Care and Research

The current health care reform effort was given momentum by the American Recovery and Reinvestment Act of
2009 (ARRA). The National Institutes of Health (NIH) received $10.4 billion in additional funding, with $1.3 billion of that going to the National Cancer Institute (NCI), to be distributed during the 2-year span of 2009 to 2010. This additional research funding was enthusiastically received by the academic research community in the hope that further federal financial support would be forthcoming to sustain the momentum that had been clearly established. ARRA funding also bolstered relatively new areas of research, including an unprecedented investment in CER, which seeks to uncover what works by comparing the clinical effectiveness, risks, and benefits of two or more medical treatments, services, and items. The use of ARRA funds to create research systems that are more efficient and interactive will help us realize the promise of research advances made possible by ARRA.

Although much of the health care overhaul legislated by PPACA is aimed at extending coverage to uninsured individuals through health insurance reform and expansion of federal health programs, it also contains several provisions that could potentially create new opportunities for the academic oncologist community (see Table 2).

Starting in 2014, health plans are required to cover routine care costs for patients in clinical trials for life-threatening diseases such as cancer. This includes dose-finding phase I trials, phase II trials to define response rates or progression-free survival, and randomized controlled trials (RCTs) in which a new treatment is compared with the standard of care. It is likely that biomarker-driven trials, which more precisely target specific tumor characteristics, will require changes in early-phase trial designs (17), require fewer patients per trial to reach molecular and clinical endpoints, and allow a more rapid "go/no-go" decision for a new antitumor agent. Because the cost to patients in clinical trials is currently a major barrier to their participation, as concluded by Klamerus and colleagues in this edition of Focus (18), the law creates the potential for increased enrollment in clinical trials. Therefore, the academic oncologist's relationship with community physicians (for potential referrals) will become increasingly important. This fact, coupled with the rapid adoption of electronic health records, which compile electronic health information from various health organizations, holds the promise to extend the reach of clinical trial participation into the community in an unprecedented way.

In the United States, the CER approach was dramatically expanded by PPACA through the establishment of an independent nonprofit center, called the Patient-Centered Outcomes Research Institute (PCORI), to prioritize and conduct research aimed at informing patient decisions. It is critical to determine early the effectiveness of a new treatment approach in a "real world" context to avoid accepting
an unproven, costly treatment as the standard of care in the absence of definitive data. High-dose chemotherapy along with autologous stem cell transplant was an accepted treatment for high-risk and metastatic breast cancer in the United States until European investigators performed the appropriate RCTs and showed that high-dose chemotherapy offers no therapeutic advantage. Academic oncologists are likely to play a central role in such comparative effectiveness studies because they typically work in an environment where data systems are used to ensure that vital clinical information is collected. Therefore, this is an area of growth and a new funding stream.

In addition, the cancer community will have ample opportunity, and indeed the responsibility, to engage in the establishment of PCORI and its ongoing prioritization processes. Specifically, oncology researchers must ensure that personalized medicine is considered in their methodologies, that a robust peer review system is developed, that an appropriate balance between evidence synthesis and evidence generation is maintained, that standards of evidence are acceptable for clinical decision-making, and that new methodologies are forward-looking and adaptive. This scientific rigor will help ensure that CER can lead to continued innovations in the health care system while eliminating unnecessary or ineffective care.

The new law also brought a new focus on translational research by authorizing the Cures Acceleration Network (CAN) within the NIH under the director’s leadership. CAN is charged with speeding the translation of basic scientific discoveries into treatments for patients, in the form of a drug, biological product, or device. The hope is that, through milestone-oriented grants to both industry and academic researchers, CAN will facilitate translational research and the development of “high-need cures” that the commercial market has little incentive to pursue. Cancer centers that promote a robust translational collaboration between basic and clinical scientists will be expected to take the lead in this novel personalized medicine approach.

The age-old adage “an ounce of prevention is worth a pound of cure” is an important theme in the health care reform law. For example, the law ensures coverage for items or services with an A or B rating by the U.S. Preventive Services Task Force. Therefore, new insurance plans will cover preventive care, including mammograms and colonoscopies, without cost sharing. In addition, the law established the Prevention and Public Health Fund for prevention, wellness, and public health activities. A significant amount of funding—$15 billion over 10 years—is available for prevention efforts, including prevention research and health screenings. The academic oncologist will want to work with officials to promote molecular and genetic approaches to prevention research. It will also be critical to leverage the investments made through ARRA and PPACA in health information technologies to track outcomes and determine which preventative measures lead to real prevention and cost savings. This evidence can also

Fig. 2. The development of personalized cancer care relies on the efforts of many people contributing to the continuous cycle of discovery, translation, and delivery of health care. The development of data networks allows for associations to be discovered between specific molecular profiles and clinical information from individual patients, leading to new knowledge that can be translated into more personalized cancer care. Comparisons of the effectiveness of diagnostics and interventions will promote clinical guidelines and ultimately improve quality and patient outcomes.
Opportunities to Reform Health Care by Using a Personalized Approach to Cancer Care

Novel health information systems

The causative genetic underpinnings of cancer have been a focus of biomedical research for decades. However, the complex interactions among multiple genes and environmental factors that contribute to the onset of cancer have hindered progress in elucidating the underlying mechanisms that lead to a cancer phenotype. New data management systems that allow cancer researchers to retrieve data sets containing disparate data that can be further analyzed with the use of computational methods will provide new insights into the mechanisms of cancer diseases.

The identification of informative diagnostic markers for cancer and its corresponding stage influences both treatment recommendations and patient outcomes, and provides further biological insights that may lead to new discoveries in drug development. Novel health information systems that focus on integrating clinical and research data linked to highly curated biorepositories (19) can be instrumental in the development of new diagnostic, therapeutic, and preventative strategies for cancer. Additionally, the information systems themselves, whether centralized or federated, will require semantic standardization using robust data dictionaries, structured vocabularies, and ontologies, and detailed metadata structures that allow for integration and harmonization of data from heterogeneous sources.

It is readily apparent that personalized medicine will require the use of observational data generated from the point of care to create well-designed RCTs that target...
specific tumor molecular characteristics to define new treatment interventions (20). The article by Christopher Booth (21) in this edition of Focus describes many of the opportunities available today to enhance RTCs, as well as the challenges involved. Today’s electronic health systems were not designed to support this type of secondary use of data to inform research, and therefore it is critical that going forward, the cancer community, and in particular academic cancer institutions, consider these factors when making decisions as to what types of information systems to implement and develop. An advantage of developing new health information systems is that it creates an opportunity to establish new data models that integrate information currently generated across silos in the health care and research enterprise. These include existing and future clinical trials; observational data from primary care of patients; surveillance data from SEER (surveillance, epidemiology, and end results), patient self-reported data; and Medicare, Medicaid, and private insurance companies to evaluate the efficacy and effectiveness of different modes of patient care. Advances in computer science, software development techniques, and a changing computing paradigm make this integration across legacy systems achievable.

The increase in the amount of data per patient through the integration of primary health care information, observational databases, and pooled trial results will strengthen our ability to learn more about the subgroups of patients who benefit from specific therapies, and influence the design of targeted validation studies (22). Therefore, a key feature in the development of the next generation of health information systems—integrating clinical, basic science, population science, biospecimen, and observational data—will be the ability to transform these data to knowledge that is consumable by rapid-learning systems for personalized cancer care. A rapid-learning system leverages recent investments in health information technology, CER, health care quality and value, and personalized medicine by integrating these approaches to produce evidence-based guidelines for clinical care, evaluate outcomes of changes in clinical practice, and generate new hypotheses for further investigation (23, 24). Although there are many issues associated with rapid-learning systems and how the integration and subsequent analyses of real-time observational data can be utilized to drive novel prospective clinical trials to validate the best personalized treatments for patients, the opportunities for improving patient care, the quality of care, and driving new healthcare innovation require the development of novel health information systems.

Design of a health information system

The design of new health information systems must overcome many current challenges, including information gaps within the health care continuum, lack of standardized nomenclatures, data standards, data quality standards, and the technical capabilities of data management architectures. First, the information gap is partially the result of how the data are collected, whether in electronic medical records (EMRs) that contain a mixture of discrete and unstructured data or in paper format. A recent survey of U.S. hospitals revealed that only 1.5% of respondents had established a comprehensive EMR to create, gather, and manage their patients’ medical care, and only an additional 7.6% had a basic system in at least one clinical unit (25). These numbers do not reflect the entire health care provider spectrum from single practitioners to medical clinics and long-term care facilities. Another hurdle is that only a small portion of patients are ever enrolled in clinical studies that strive to capture information on risk factors, quality of life, or other patient-centric parameters that are essential for personalized medicine. Second, although many nomenclatures and data standards exist (e.g., SNOMED CT, ICD-9-CM, MedDRA, LOINC, and GO) few health care organizations have created strategies to adopt these standards across their information technology infrastructure, and even when they do, they often implement them differently. Third, the lack of data quality standards makes it challenging to interpret and use data outside of the context in which they were captured. Finally, the architectures of health information systems will need to share data between health care providers and consumers to facilitate personalized medicine and patient-centered outcomes research. Currently, the two main architectures are the centralized and federated data models. Each has distinct benefits and risks, with the centralized model facilitating stronger secondary uses of data and the federated model enabling more efficient linkage of information and arguably better security of patient information. However, the need to consolidate and link many disparate types of data from numerous sources will likely require an integration of both models, i.e., a network model (Fig. 3), to produce robust information systems that can support a broad audience and take advantage of genotypes, phenotypes, and other patient data to realize the potential of personalized medicine.

Several projects have laid some of the foundation for creating this next generation of federated health information systems. One project, the cancer Biomedical Informatics Grid (caBIG), resulted in data standards and software tools that facilitate the sharing of data (molecular, clinical trials, biospecimens, and other clinical data) via a federated architecture (26). caBIG has been the foundation for other projects, including The Cancer Genome Atlas, the Repository of Molecular Brain Neoplasia Data, and the National Health Information Network. Many other information-system projects are under way to build the infrastructure required to support personalized medicine (27). One example is the development of a database for CER based on a prospective study being conducted at 19 sites throughout the United States and based at the Moffitt Cancer Center (28). This database is being designed to integrate observational and clinical trial data, and will provide users with new tools for accessing and using data for patient-centered outcomes research. One of the benefits of unifying current and evolving data infrastructures into a
network model is that the resulting data management system can serve as a prototype for testing personalized medicine use cases and exploring the utility of these resources for the development of new therapies.

**Network model use cases**

The following "use cases" illustrate how the development of integrated data networks can be beneficial to critical stakeholders, including researchers, clinicians, health care policy makers, and, of course, patients themselves. Data from many sources, including genomic databases, EMRs, laboratory and imaging files, and claims databases will need to be interoperable to enable information from these different sources to be normalized, integrated, and related, and associations made through analytics to drive new insights. This should result in new knowledge leading to new diagnostic and treatment discoveries, clinical decision support tools, improved outcomes based on CER, and reduced health care costs based on HTA. Below are a number of use cases that would be enabled by the network information model contemplated here:

1. A primary care hospital is creating a personalized health record (PHR) portal for its cancer patients that contains data corresponding to each patient’s disease history and allowing the patient to add additional risk assessments, past medical history, and family history data. The PHR portal is a "living diary" of each patient’s medical history that is available to the patients and their caregivers electronically. The network model allows the primary care hospital to link to local oncology offices and clinics to capture offsite treatments, PHR sites (HealthVault, WebMD, familyhistory.hhs.gov, etc.) where patients may already have accounts, and health information exchanges (HIE) to create a comprehensive record. Using these resources, the patient can exchange and share these data with other health care providers connected to the data management network. This is particularly relevant for following and providing optimal care to cancer survivors, who have been described as a population that has been "lost in transition." (29)

2. A research team is exploring the molecular mechanisms of pancreas cancer to discover circulating serum biomarkers that have a strong correlation with early-stage disease and possible new drug targets. The team is using a systems biology approach to identify perturbed pathways associated with early-stage pancreas cancer, which requires several well-annotated, high-
quality biospecimens for multiple molecular analyses. The multi-institutional team has limited resources for the project. The network model provides a wealth of resources. The team is able to identify biospecimens that are available from appropriate patients at other research centers, and obtain data from multiple molecular platforms in public repositories. As the research team analyzes the molecular data, they can use other parts of the data network (including the results of previous biomarker-driven clinical trials in pancreas cancer) to gain new insight into disease processes, detect early disease biomarkers, and discover new drug targets.

3. A large health care network wants to compare multiple treatment modalities for several different cancers to determine the most effective treatments based on genetic stratification with CER methodologies. This comparison is based on data gathered through a national consortium of sites participating in a lifelong observational study on cancer. The analysis would include data mining of the observational data available throughout the network, including insurers, HIE, PHR, and clinical data sources. By exploring these data, researchers can identify clinically relevant subpopulations (including treatment responders and nonresponders) along with the effectiveness and toxicities of specific combination therapies. With the available molecular-based data resources, they can augment a CER study by using genetic markers to further stratify patients. The combination of these data would aid in the development of evidence-based guidelines for matching the right patient to the right treatment at the right time. The network data model provides the foundation for CER to more accurately derive information that will lead to novel models of care that may dramatically improve patient care. A key feature of this design is the inclusion of community medical centers and physicians as true partners in CER, so that effectiveness can be measured in the real world. (30)

4. The Agency of Healthcare Research and Quality is interested in funding numerous studies that will provide evidence to improve outcomes and safety for outpatient infusion centers throughout the United States. This evidence will be primarily used for comparative effectiveness and HTA to create new policies that will define quality-of-care metrics and influence reimbursement strategies as part of health care reform. The network data model provides the foundation for the conduct of these studies through the integration of insurers, health care providers, research centers, and the ability to reach out to the patient community. The sheer scale of the network enables researchers to capture trends across the health care enterprise, and to generate statistically relevant data sets to facilitate new policy decisions in a time frame that would not be feasible with traditional RCTs or other prospective-based studies.

New Clinical Trial Approaches

Investigators today also have the opportunity to create innovative clinical trial designs by leveraging advances made in the last decade in molecular profiling and the electronic health infrastructure. In March 2010, the NCI Operational Efficiency Work Group released its findings regarding the activation of CTEP-sponsored phase II trials and Cooperative Group phase II trials to the Clinical Trials and Translational Research Advisory Board (31). This report, as well as the Institute of Medicine report entitled “A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program,” led to serious concerns about the conduct of clinical research in cancer in the United States (32). The results demonstrate that the median times to activation of phase II and III trials are 550 and 830 days, respectively, and that 58% and 23% of phase II and III trials, respectively, require more than 2 years to activate. Note that this refers only to the activation of the trial and does not include the time needed to complete the study. These findings prompted the NCI to issue more stringent timelines for the activation of phase II and III trials: 210 and 300 days, respectively, with firm termination deadlines of 18 and 24 months, respectively. Although these timelines, if achieved, will significantly improve the activation of later-phase clinical trials, it is likely that novel trial designs and the participation of a large network of cancer centers, community doctors, and hospitals will further improve the activation and conduct of clinical trials. Recent articles in CCR Focus described novel phase II trial designs and the effective incorporation of biomarkers in these trials (33–36). For example, a comprehensive cancer center that oversees a network database containing molecular and clinical data on significant subgroups of patients would be poised to efficiently activate and conduct a biomarker-adaptive, parallel, two-stage design trial within that network. The ability to collect real-time patient clinical data and tumor molecular profiles across a large network would facilitate the rapid conduct of a phase II trial that includes an integral biomarker analyzed in a Clinical Laboratory Improvement Amendments laboratory (37). Selection of patients with this biomarker (either a subgroup of patients with the same disease histology or across disease types) would allow for a proof-of-concept trial requiring fewer subjects who have been enriched for the biomarker.

Conclusions

In this Focus review, we describe specific aspects of PPACA that will influence how cancer research and care are conducted in the future. The time for “team science” has never been greater. Primary stakeholders in health care reform, including researchers, clinicians, policy makers, patients and patient advocacy groups, and pharmaceutical companies, must come together to organize the framework and environment to promote personalized medicine. It is unrealistic to expect any one stakeholder to collect the
resources needed to create rapid-learning information systems that can take advantage of current and past information and translate it into usable knowledge to improve patient care. A national personalized medicine program for cancer requires the creation of regional consortia that collect patient-level data (e.g., clinical, environmental, risk factor, molecular, and outcomes data) and focus on specific classes of disease, develop research methodologies, create validation networks, and encourage partnerships with industry leaders, especially in biotechnological, pharmaceutical, and information systems. This will be an effective strategy for defining and implementing improved standards of care using a team science approach. Many different areas of invested stakeholders, including comprehensive cancer centers, primary care facilities, community medical centers, and research institutions, are poised to make an extraordinary impact on health care focused on the acute and chronic aspects of cancer diseases through partnerships and resources that have been evolving during the past decade. Indeed, a case can be made that regional approaches are necessary to identify the needs of specific populations and to address underserved populations. New infrastructure, broad expertise across the health care and research spectrums, and an unprecedented effort to reach all corners of the health care industry will be required to exploit the advantages of this necessary team-science approach to fighting cancer.

For these teams to function optimally, an expanded health information infrastructure will be required, including hardware, software, and personnel to create a robust and scalable information integration platform for use by all team members and stakeholders. Indeed, it will be important to consider the needs of each constituent in developing portals to the integrated information system. For example, the presentation of new information and knowledge generated by the network will be very different for patients building their own personalized health record compared with cancer researchers pursuing new biomarker discoveries. To fully leverage the information technologies, frontier scientists and researchers focused on developing personalized medicine technologies and methodologies will need to be a focal point of these efforts. In complement to the scientific infrastructure, additional resources will be required to expand information systems to community hospitals and physician practices such as dedicated biomedical informatics and IT professionals. By investing in these areas, we can capture more complete data about each cancer patient to create a health care network that can validate personalized medicine methods at the sites of patient care. This undertaking will require new partnerships to help develop low-cost, low-maintenance health information systems that provide value to the healthcare industry without unrealistic overhead. Ultimately, the establishment of rapid-learning, knowledge-based health systems will improve quality by enabling the best options for patients to be determined based on evidence; accessibility by providing key information to teams of caregivers; and affordability by reducing the use of ineffective and unnecessary diagnostics and therapies.

Disclosure of Potential Conflicts of Interest

W.S. Dalton received a commercial research grant from Merck and is a chairperson of M2-Gen, a for-profit company in personalized medicine. The other authors disclosed no potential conflicts of interest.

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